To enhance clinical care and move research forward in Sjögren’s, the Sjögren’s Syndrome Foundation (SSF) has set the development of Novel Diagnostics as a top priority for its 2013 research program. (To learn more about the SSF Research Program, how to apply, and 2013 priorities for awards, visit www.sjogrens.org/research.) The SSF kicked off the announcement of this priority with a program focused on Novel Diagnostics at the SSF annual luncheon meeting during the American College of Rheumatology conference in November. “Better and more precise ways are desperately needed to diagnose and monitor Sjögren’s patients,” says SSF CEO Steven Taylor. “Advocating for improved diagnostics is an important part of our Foundation’s strategy for meeting the SSF Five-Year Breakthrough Goal – To shorten the time to diagnose Sjögren’s by 50% in five years!”

Held in Washington, D.C., the SSF meeting at ACR brought about 80 clinicians and researchers who packed the room to hear about new concepts in the pipeline. SSF Medical and Scientific Advisory Board Chair Denise Faustman, MD, PhD encouraged attendees to think about new targets that could be explored for diagnosis: “It’s time this disease moved away from an invasive procedure – the lip biopsy, and that we came up with a non-invasive ‘gold standard’ for identifying Sjögren’s patients. A simpler, more decisive diagnostic test will help everyone – patients, clinicians, researchers and insurers, and it will lead to earlier diagnosis...”

Continued on page 2 ▼

Emerging Evidence May Lead to Hope for Early Detection and Intervention for Sjögren’s

by Stephen Hsu, PhD1,2,3, Douglas Dickinson, PhD3, and Scott DeRossi, DMD2

1 Department of Oral Biology; 2 Department of Oral Medicine and Diagnostic Sciences, College of Dental Medicine; 3 College of Graduate Studies Georgia Health Sciences University, Augusta, Georgia

Sjögren’s syndrome (SS) affects 1-3% of the population in the United States.1 Complications resulting from SS significantly decrease quality of life. If the onset of autoimmune disorders such as SS could be diagnosed at a stage prior to the appearance of symptoms, then more therapeutic options could be developed to prevent and delay the onset of disease. Unfortunately, the pathogenesis of this disease is poorly understood. This has made early detection, prevention and intervention prior to the onset of overt...
Four presenters offered glimpses of a better future in diagnostics. The meeting during ACR was made possible by support from Immco Diagnostics (http://immco.com) and Genalyte, Inc. (www.genalyte.com). Synopses of the meeting presentations follow.

**Novel Biomarkers for Early Diagnosis**

by Lakshmanan Suresh, DDS, MS

Vice President of Research & Development and Clinical Services, Immco Diagnostics, Inc., Buffalo, New York

The discovery of novel antibodies in Sjögren’s syndrome (SS) by the University of Buffalo is expected to lead to earlier diagnosis and subsequently earlier treatment of Sjögren’s patients. Led by Julian L. Ambrus Jr., MD, Professor, University of Buffalo Department of Medicine, and whose group has partnered with Immco Diagnostics, Inc., the breakthrough could mean the availability of new assays for a routine diagnostic test as early as 2013. The newly identified antibodies were positive in many Sjögren’s patients who were not positive for anti-SSA/Ro and anti-SSB or La, broadening the number of patients who could be more easily diagnosed. One specific antibody was positive in a majority of patients and in those who had had symptoms of Sjögren’s for less than two years, making this marker particularly important for early diagnosis.1

Early diagnosis of SS is important so that glandular function might be preserved and complications such as lymphoma prevented. Currently no sensitive test exists for early detection of SS. The diagnosis of SS is difficult because of the diverse clinical presentation. In addition, the current diagnosis provisionally recommended by the American College of Rheumatology is based on multiple criteria including a combination of blood tests for multiple biomarkers, minor salivary gland biopsy and ocular stains. Current criteria for diagnosis of SS may appear much later at a time when the salivary and lacrimal glands may not be amenable to recovery with appropriate treatment. Hence, a dire need exists for an early and sensitive marker for diagnosis.

Researchers have been trying to identify early sensitive and specific markers for SS using mouse models. Interleukin-14 alpha transgenic mice (IL-14 ATG) is one such model and reproduces all the features of SS seen in patients, in the same relative time frame.2,3 The IL-14A TG mouse hypergammaglobulinemia, autoantibodies, loss of salivary and lacrimal gland function with lymphocytic infiltration of the glands, interstitial lung disease, mild renal disease and in old age B cell lymphomas.2,3 Hence the IL-14ATG mouse is an ideal model to study the early events leading to salivary gland injury in SS and to identify markers that may be used to diagnose disease earlier in humans. Using this model, researchers at the University of Buffalo and IMMCO have determined that salivary protein-1 (Sp-1), parotid specific protein (PSP) and Carbonic anhydrase VI (CA6), all localized in the exocrine glands, may be useful as early biomarkers of SS and allow identification of salivary and lacrimal gland destruction at a time when it may still be amenable to current treatment options.4

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**Graph: Sensitivity of SS autoantibody markers in patients with dry mouth and dry eyes**

<table>
<thead>
<tr>
<th>Autoantibody Markers</th>
<th>Percent Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ro/La</td>
<td>80%</td>
</tr>
<tr>
<td>SP-1</td>
<td>70%</td>
</tr>
<tr>
<td>CA6</td>
<td>50%</td>
</tr>
<tr>
<td>PSP</td>
<td>40%</td>
</tr>
<tr>
<td>SP-1/CA6</td>
<td>20%</td>
</tr>
</tbody>
</table>

The early biomarkers described above were present in two animal models for SS and occurred earlier in the course of the disease than antibodies to Ro or La.
Patients with SS also produced antibodies to SP-1, CA6 and PSP. These antibodies were found in 45% of patients meeting the criteria for SS who lacked antibodies to Ro or La. Furthermore, in patients with idiopathic xerostomia and xerophthalmia for less than 2 years, 76% had antibodies to SP-1 and/or CA6 while only 31% had antibodies to Ro or La. Antibodies to SP-1, CA6 and PSP may be useful markers for identifying patients with SS at early stages of the disease or those who lack antibodies to either Ro or La. These antibodies are found at a very early stage of the disease and hence help in therapeutic interventions that may be helpful in the restoring of glandular function.

References

Looking at Cell Proteins for Faster Sjögren’s Syndrome Diagnosis

by Denise L. Faustman, MD, PhD
Assoc. Prof. of Medicine, Harvard Medical School; and Director, Immunobiology Laboratory, Massachusetts General Hospital, Charlestown, Massachusetts

Sjögren’s syndrome today remains very difficult to diagnose, taking an average of 6.5 years from onset of symptoms. Part of this difficulty lies in the fact that there is currently no single test available that is sensitive or specific enough to make a definitive diagnosis of Sjögren’s. In addition, symptoms vary from patient to patient, and many are not specific to Sjögren’s alone. Instead, Sjögren’s is often initially mistaken for another condition or simply undiagnosed. This means that early diagnosis, which could help prevent or ameliorate many of the symptoms and long-term complications of this disease, is rare.

Diagnosis of Sjögren’s is based on a combination of symptoms, blood tests, tissue studies, and physical exam. Unfortunately, tissue studies—in other words, biopsy—can have a high rate of false negative results. Indeed, misdiagnosis or nondiagnosis is estimated to occur with nearly half (45%) of biopsy specimens from patients with Sjögren’s. This can easily lead to patient frustration, disease progression, and escalating medical costs as patients continue to search for the cause of their symptoms. Biopsies are also more invasive than a simple blood test and rarely do patients want to have the procedure performed on more than one occasion.

All of this would likely be exacerbated by proposed new requirements for yearly repeats of biopsy to maintain a Sjögren’s diagnosis. According to proposed changes to the current Sjögren’s diagnostic guidelines, a patient with dry mouth symptoms would have to have a positive lip biopsy to be considered to have Sjögren’s, and the biopsy would possibly have to be repeated to maintain the diagnosis. Unfortunately, such diagnostic guidelines would likely dramatically increase the rate of missed diagnoses, since there is a significant false-negative rate associated with lip biopsies, which can miss small, early sites of inflammation, even inflammatory sites in moderate disease or no signs of inflammation in late disease when the gland is destroyed and fibrosis might be the primary observation.

Clearly, better, more specific tools for Sjögren’s diagnosis are needed to improve the early detection and treatment of this disease—and, in doing so, help to prevent complications, reduce patient anxiety, and reduce healthcare costs.

One possibility for improving the diagnosis of Sjögren’s lies in looking at certain proteins in the white blood cells. Early research from the Massachusetts General Hospital (MGH) Immunology Lab showed that, in the mouse model of Sjögren’s, the LMP2 protein is either missing or present at only very low levels, resulting in progression towards autoimmunity. This protein is necessary for proper T cell education—that is, for the cells of the immune system to accurately recognize the body’s own cells as “self” and not “foreign.” Importantly, these findings about low to undetectable LMP2 levels in mice have since been demonstrated in humans by researchers in Germany. Krause and colleagues have shown that humans with primary Sjögren’s syndrome have reduced LMP2 normally found in white blood cells. This same defect is not observed in other autoimmune diseases, including lupus and rheumatoid arthritis, nor is it found in healthy people.

Based on the work of all of these groups, we believe it is possible to develop a diagnostic for primary Sjögren’s based on detection of the LMP2 protein in a standard blood sample. Moving to non-invasive, specific, protein-level detection methods—rather than surgical methods such as a lip biopsy or other non-specific ways tests currently used—would be an important advancement that would allow for earlier and more accurate Sjögren’s diagnosis.

Continued on page 4 ▼
Development of a more specific diagnostic for Sjögren’s will also contribute to reducing healthcare costs by ensuring more patients are treated earlier in the course of their disease, which can help stave off disease progression and the onset of more severe complications. If successful, such an assay could lead to a specific diagnostic test for primary Sjögren’s, addressing the clinical need to more precisely diagnose the disease, and at earlier time points.

References

What role might salivary gland ultrasound (SGUS) play in the diagnosis of Sjögren’s, and could this diagnostic tool be used to replace more invasive and expensive methods currently in use? Dr. Bowman provided the evidence to-date and led a discussion on the potential inclusion of SGUS in diagnostic criteria for Sjögren’s.

Conclusions drawn from recent studies demonstrate that salivary gland ultrasound certainly can and probably should be added to the diagnostic arsenal – at least as a first-line imaging tool. Sensitivity and specificity of SGUS is high and correlates closely to that of sialography (Tables 1 and 2).1,4 Comparable levels of accuracy also were found in two studies evaluating SGUS versus the lip biopsy.5,9

However, while ultrasound might provide a viable alternative to sialography and perhaps even the lip biopsy, further investigation is needed. For example, agreement must be obtained on a scoring system, as different systems currently are in use to gauge ultrasound results. In addition, while ultrasound can be used to examine the salivary gland for a wide range of variables, including size, echogeneity, homogeneity (or uniformity), heterogeneity/inhomogeneity, hypoechoic areas, hyperechoic reflectivity, border clarity and vascularity, the relative validity of each needs to be determined. Cornec et al (2013)8 most recently found that the receiver operating characteristic (ROC) curve analysis was most useful, while gland size measurement and Doppler waveform were less so. Finally, the clinical value of SGUS should be established in Ro/La negative patients.

While it was pointed out during discussion that no current test matches the ability of the lip biopsy to examine focal lymphocytic infiltrates and thus as a “gold standard” for diagnosing Sjögren’s, the accuracy of visualizing structural changes in the salivary gland has reached a high level with modern-day ultrasound. Salivary gland ultrasound now may be viewed at the very least as an additional diagnostic tool and even as a viable alternative to sialography. It also may become an initial diagnostic tool that ultimately could replace the lip biopsy or at least be used unless and until a lip biopsy is determined to be crucial for diagnosis, the circumstances for which would then need to be defined.

Table 1: Sensitivity and Specificity of Salivary Gland Ultrasound

<table>
<thead>
<tr>
<th>Study (Scoring System)</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Niemela 2004 (0-4)</td>
<td>78</td>
<td>94</td>
</tr>
<tr>
<td>Hoccevar 2005 (0-48)</td>
<td>59</td>
<td>99</td>
</tr>
<tr>
<td>Poul 2008 (0-16)</td>
<td>84</td>
<td>73</td>
</tr>
<tr>
<td>Salaffi 2008 (0-16)</td>
<td>75</td>
<td>84</td>
</tr>
<tr>
<td>Takagi 2010 (0-4)</td>
<td>68</td>
<td>83</td>
</tr>
<tr>
<td>Milic 2010 (0-12)</td>
<td>90</td>
<td>95</td>
</tr>
<tr>
<td>Milic 2012 (0-16)</td>
<td>91</td>
<td>94</td>
</tr>
<tr>
<td>Cornec 2013 (0-4* &amp; 0-16)</td>
<td>63</td>
<td>95</td>
</tr>
<tr>
<td></td>
<td>*also cf MRI (SN=81%) and MR sialography (SN=96%)</td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Salivary Gland Ultrasound Compared to Sialography

<table>
<thead>
<tr>
<th>Study</th>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salaffi 2008</td>
<td>sialography</td>
<td>73</td>
<td>85</td>
</tr>
<tr>
<td></td>
<td>ultrasound</td>
<td>75</td>
<td>84</td>
</tr>
<tr>
<td>Takagi 2010</td>
<td>sialography</td>
<td>78</td>
<td>82</td>
</tr>
<tr>
<td></td>
<td>ultrasound</td>
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<td>83</td>
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<tr>
<td>Poul 2008</td>
<td>sialography</td>
<td>78</td>
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</tr>
<tr>
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<td>ultrasound</td>
<td>84</td>
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<tr>
<td>Milic 2009</td>
<td>sialography</td>
<td>67</td>
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</tr>
<tr>
<td></td>
<td>ultrasound</td>
<td>87</td>
<td>91</td>
</tr>
</tbody>
</table>

References
Multiplex Analysis of Autoimmune Markers Using Silicon Photonics

by Martin Gleeson, PhD, Chief Scientific Officer, Genalyte, Inc.

Dr. Gleeson announced the development of a new immunoassay that takes advantage of silicon photonics and is expected to come onto the market for commercial use in 2013 and for private offices in the near future. Calling the Maverick equal or superior to ELISA, Dr. Gleeson explained the benefits of multiplexing technology to the clinical and research communities as one that will allow physicians to more easily test for multiple markers to make a diagnosis and assess a patient for multiple autoimmune conditions at one time. In addition, the Maverick allows for a substantial reduction in preparation time, labor and reagents. Many of the commercially available technologies currently on the market (ELISA, Lumineo®, flowcytometry, western blot, IFA) lack multiplexing capability and/or are labor intensive.

Silicon photonics has a successful track record after being used routinely in the telecommunications industry for years, and the methodology now has been employed by high-resolution mass spectrometry coupled with bioinformatic tools to identify biomarkers. MALDI O-TOF MS analyses of saliva samples were highly reproducible and the mass spectra generated were very rich in peptides and peptide fragments in the 750-7,500 Da range.

Data analysis using bioinformatic tools resulted in several classification models being built and several biomarkers identified. One model based on 7 putative biomarkers yielded a sensitivity of 97.5%, specificity of 97.8% and an accuracy of 97.6%. One biomarker was present only in SjS samples and was identified as a proteolytic peptide originating from human basic salivary proline-rich protein 3 precursor. We conclude that salivary biomarkers detected by high-resolution mass spectrometry coupled with powerful bioinformatic tools offer the potential to serve as diagnostic/prognostic tools for SjS.
symptoms impossible to date. Thus, from a medical perspective, the current focus on SS is largely diagnosis (which itself may take many years) and treatment of symptoms, not the underlying disease. Current standard of care is unable to address disease progression.

For the treatment of symptoms, the first generation of agents developed consists of over-the-counter products aiming to moisturize the oral lining or to deliver agents that can be helpful in reducing the oral health effects of dry mouth. These include xylitol, a naturally occurring sugar-alcohol, and certain antimicrobial salivary enzymes. Although generally well-tolerated, these agents require continuous application. The next generation comprised prescription medications that provide pharmaceutical stimulation to the salivary gland cells. These were approved by the FDA more than a decade ago and are associated with many adverse side effects such as sweating, diarrhea and cardiac complications and poor patient compliance. Thus, currently used approaches are all aimed at temporary relief of certain symptoms without addressing the root of the problem—the gradual loss of function in the salivary gland cells due to the lack of knowledge of when and what triggers the change in the salivary glands.

Clinicians and researchers understand that the initiation of disease, the incubation period, could last for years (and perhaps decades). Most existing theories for the origin of SS hold that abnormalities in the innate immune system play the key role in disease pathogenesis. The immune system’s action on the glands leads to salivary dysfunction (and other abnormalities) caused by the loss of function of glandular cells and eventually cell loss through immune system-induced cell death.2 In these theories, the salivary glands themselves are initially normal and their cells are simply bystanders. Based on these ideas, immunosuppressant and other therapies targeting the immune system as a whole were developed to manage the disease. Unfortunately, these relatively indiscriminate therapies are associated with increased risk for infection, cancer and other long-term consequences.

Recently, researchers found that the salivary gland epithelial cells themselves play a key role in both the onset and continuation of this autoimmune disorder.2,3 One proposed mechanism points to the glandular epithelial cells as the source of initial events.4 The involvement of salivary gland cells in the pathogenesis of SS is an exciting phenomenon, because it suggests that the immune system might simply perform its “normal” function: to clear molecules it recognizes as “foreign” by attacking the targets with cytokines, antibodies and “killer” cells. However, although altered expression of various genes and proteins has been found previously in SS patients, these alterations occur long after the appearance of overt symptoms.

Therefore, we initiated an effort to search for changes in the salivary gland cells prior to disease onset, first in animal models, then in human samples obtained from SS patients. Our group has also focused on plant-derived natural antioxidants for the protection of secretory glands. One group of these natural and non-toxic compounds is obtained from a popular beverage in East Asia: green tea. Epidemiologic studies indicate that genuine differences in the prevalence of SS among various regions and communities exist. In China, one study suggested the prevalence of primary SS was 0.03%, whereas serological screening showed 0.33% prevalence of primary SS (Fox criteria).2 In Japan, the estimated crude prevalence rates for SS were only 1.9 and 25.6 per 100,000 in males and females, respectively.7 A survey conducted by the Japanese Ministry of Health and Welfare indicated the SS prevalence was just 0.06% among females.8 Although there is a lack of direct statistical comparison between the U.S. population and either the Japanese or Chinese population, it is apparent that SS and xerostomia are significantly more prevalent in the U.S. population. Noticeably, China and Japan have the largest populations of green tea consumption.

Our group previously found that autoimmune-associated symptoms (SS, psoriasis, type-1 diabetes) in animal models can be managed by certain molecules present in green tea leaves.9,10 The most recent findings from our group, published in the journal of Autoimmunity, described a longitudinal study using the NOD.B10. H2-B mouse model for human primary SS.4 The study design investigated changes in the salivary gland and pancreas at several time points when the animals are characterized as “healthy” — that is, before the appearance of lymphocytic infiltration in the salivary glands (a characteristic sign for SS).

Remarkably, as early as 6 weeks old, these animals showed significant oxidative DNA damage and DNA repair activities in the salivary gland in comparison to control mice, BALB/c, that do not develop SS-like disease. These oxidative stress-induced abnormalities continued to increase through an 8-week period, during which a significant decrease in a key antioxidant defense enzyme, peroxiredoxin 6, became apparent. On the other hand, animals fed with EGCG, a major component of green tea antioxidants, showed significantly less oxidative DNA damage. In addition, in EGCG-fed animals, levels of a DNA repair marker PCNA (proliferating cell nuclear antigen) and the antioxidant enzyme peroxiredoxin 6 were similar to the normal control counterparts. These results suggest that during a long period in which animals are otherwise categorized as “healthy,” oxidative stress was increasing to damaging levels in the salivary gland and gradually causing increased oxidative damage to vital molecules such as DNA. If the oxidative stress...
continues to elevate, the antioxidant defense enzyme system could be compromised, leading to extensive oxidative damage or structural modification to vital molecules, including DNA, RNA, lipids and proteins. In turn, this may result in apoptosis (programmed death) of cells that accumulated damage beyond repair. Importantly, when these molecules are in their abnormal oxidative form and exposed to the immune system during degradation of a cell, the immune system may misrecognize these molecules as “foreign” and mobilize a powerful but normal immune reaction against them, causing injury to the salivary gland (or the pancreas), including additional oxidative damage. Consequently, a vicious feedback loop forms that sustains an immune attack on the tissues, leading to more lymphocytic infiltration, inflammation, and loss of function.

A potential argument is that events observed in mice may not happen in the human body. However, similar results were found in salivary tissues obtained from SS and xerostomia patients. In humans, the immune system and the antioxidant system are two vital defense systems in our body. The antioxidant defense system is constantly engaging oxidative stress from free radicals either produced by our own mitochondria, or from medication, radiation, chemicals, or even food components. This system consists of many inducible or constitutively expressed enzymes such as glucose-6-phosphate dehydrogenase (that produces NADPH, a reducing agent), glutathione peroxidase, catalase, peroxiredoxin (that convert hydrogen peroxide to water), and superoxide dismutase (which converts toxic superoxide to less toxic hydrogen peroxide), etc., in order to protect cells and tissues from oxidative damage. Our group reported that in SS patients and xerostomia patients, peroxiredoxin 6 and glutathione peroxidase 1 are significantly lower and PCNA levels are significantly higher than healthy individuals. These results indicate that similar to the mouse model, the down regulation of the antioxidant defense enzymes may be the result of an undetected “incubation” period that lasts for years. However, an encouraging finding is that when cultured human salivary gland cells are exposed to EGCG, the protein level of peroxiredoxin 6 is increased many times, which matches the animal data.

Our current effort is to identify biomarkers for the early detection of abnormalities that could lead to autoimmune disorders such as SS and type-1 diabetes, ideally years ahead of any detectable symptom, and to investigate prevention and intervention using plant-derived, non-toxic natural compounds. A double-blind, placebo-controlled, randomized clinical trial will soon be completed in our university’s College of Dental Medicine using a natural formula containing plant extracts (including green tea extract) and an appropriate amount of xylitol to evaluate it as a new generation of potential therapeutic medications.

In conclusion, with newly emerged discoveries, it is time to revisit the decades-old theories, approaches, medications, and symptom-relief products for the pathogenesis of autoimmune disorders such as SS and the approaches for diagnosis and treatment/management. In the near future, we may be able to detect signs for autoimmune disorders when individuals are apparently completely “healthy,” and we could design approaches to prevent or delay the onset of autoimmune diseases for years or even decades. Future research directions also should include the identification of the
12th International Symposium on Sjögren's Syndrome

New Era on Sjögren's Syndrome
Attention for Sjögren’s at ACR Increases Dramatically

Sjögren’s was highlighted more than ever before at the American College of Rheumatology (ACR) annual meeting held in November in Washington, D.C. “We are pleased that our relationship with the ACR continues to grow, increasing opportunities to educate rheumatologists and encourage researchers in Sjögren’s,” says Steven Taylor, SSF CEO. Sessions on Sjögren’s at ACR included:

- The Foundation-led presentation on the SSF Clinical Practice Guidelines initiative with Moderator Frederick Vivino, MD and presenters Steven Carsons, MD and Ann Parke, MD. Speakers discussed the rigorous process underway as the Foundation has been tackling key clinical questions in the management and treatment of Sjögren’s. A full article covering this topic will appear in a future issue of the *Sjögren’s Quarterly*.

- A presentation on the 2012 ACR Classification Criteria for Sjögren’s moderated by Lindsey Criswell, MD, MPH, Dsc with Stephen Shiboski, PhD presenting.

- An SSF-hosted discussion meeting entitled “Criteria in Sjögren’s – Steps Forward” and chaired by Caroline Shiboski, DDS, PhD and Xavier Mariette, MD. While the American European Consensus Group criteria has been in wide use by investigators worldwide since 2002, ACR recently provided tentative endorsement of new criteria developed by the Sjögren’s International Collaborative Clinical Alliance (SICCA) Registry and published in 2012. The international community came together to discuss ways to ensure international collaboration as criteria is validated and refined. A meeting summary along with steps forward that were delineated will be published in the 2013 spring issue of the *Sjögren’s Quarterly*.

- The SSF luncheon meeting on Novel Diagnostics that packed more attendees than at any previous meeting. See cover story in this issue of the *Sjögren’s Quarterly*.

- The Sjögren’s Syndrome Study Group led by Jacques-Eric Gottenberg, MD. The study group covered “From Pathogenesis to New Therapeutic Perspectives of Primary Sjögren’s Syndrome.”

- Two “Meet the Professor” sessions on “Controversies in Sjögren’s” led by Alan Baer, MD.

- A Curbside Consult on “Sjögren’s Syndrome: Challenges in Clinical Practice” led by Frederick Vivino, MD.

- Two oral poster sessions and a poster tour on Sjögren’s. The number of abstracts on Sjögren’s submitted to ACR tripled and the number accepted nearly doubled to 76 this year. Oral presentation sessions on selected abstracts doubled to two with one on clinical aspects of Sjögren’s moderated by E. William St.Clair, MD and Athanasios G. Tzioufas, MD and a second session on Pathogenesis and Sjögren’s moderated by Xavier Mariette, MD, PhD and Lindsey A. Criswell, MD, MPH, Dsc. In addition, a Poster Tour in Sjögren’s was scheduled and led by Jacques-Eric Gottenberg, MD.  

Continued on page 10

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Special offer for SSF members
Every year, the Sjögren’s Syndrome Foundation (SSF) recognizes the best abstract at the American College of Rheumatology (ACR) annual meeting by an investigator who is early in his or her career. Highlighting excellent research and promise for the future is an important goal of the SSF Research Program. This year was a particularly competitive year for the abstract award as the number of ACR abstracts presented on Sjögren’s nearly doubled compared to previous years.

This year’s winner of the SSF Outstanding Abstract Award is Hongen Yin, MD, PhD of the National Institute of Dental and Craniofacial Research (NIDCR), National Institutes of Health (NIH), Bethesda, Maryland. Dr. Yin was recognized for her abstract entitled “Overexpression of BMP6 Is Associated with Loss of Salivary Gland Activity in Sjögren’s Syndrome Patients and Mice.”

Dr. Yin’s study focused on changes in the epithelia associated with the loss of gland activity and identified BMP6 as a novel gene linked with xerostomia in Sjögren’s. Overexpression of BMP6 was found to induce loss of salivary and lacrimal gland function in mice, a finding that was further supported in patients. This discovery offers a potential new target for therapeutic intervention in Sjögren’s and also suggests that pro-inflammatory cytokines, separately from Sjögren’s autoantibodies, are associated with loss of salivary gland function in Sjögren’s. Abstract co-authors include Javier Cabrera-Perez, Zhennan Lai, Drew Michael, Melodie Weller, Bill Swaim, Noreen Rana, Xibao Liu, Ilias Aleviszos, Indu Ambudkar and John A. Chiorini, all from the NIDCR, NIH, Bethesda, Maryland.

Sometimes an additional abstract ranks a close second and receives such high praise that the SSF decides to also award an Honorable Mention. That was the case this year with Chang-Fu Kuo, MD, who was recognized for his abstract entitled “Sibling Relative Risk and Heritability of Sjögren’s Syndrome: A Nationwide Population Study in Taiwan.” Based at Chang Gung Memorial Hospital in Taiwan, Dr. Kuo is currently engaged at the University of Nottingham in the U.K. He and colleagues examined familial relative risk (RR) and heritability of Sjögren’s in the general population of Taiwan using data from that country’s National Health Insurance Research Database. Siblings of those with Sjögren’s were more likely to develop the disease than those without at an RR of 15.51 (95% CI, 5.85–41.12), and the heritability of Sjögren’s was gauged at 0.54 (95% CI, 0.32–0.80). The first population-based study on Sjögren’s demonstrated a clustering of the disease in families and suggests a significant genetic contribution to its development.

In addition to lead author and presenter Dr. Kuo, abstract authors include Matthew J. Grainge, Kuang-Hui Yu, Lai-Chu See, Shue-Fen Luo, Ana M. Valdes, I-Jun Chou, Hsiao-Chun Chang, Weiya Zhang and Michael Doherty and with representation from the University of Nottingham, U.K., Chang Gung Memorial Hospital and Chang Gung University in Taiwan, and St. Thomas’ Hospital, King’s College London.

For full abstracts, visit www.sjogrens.org/research and select “Outstanding Abstract Award.” Awardees received a framed certificate and the winner a US$500 check during the annual SSF luncheon meeting during the ACR in November 2012. The SSF is indebted to a wonderful group of experts who volunteer their time to make up the SSF Research Review Committee to determine awardees and help us recognize up-and-coming investigators.

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Do we have your e-mail address?

If you want to receive all the latest updates from the Sjögren’s Syndrome Foundation, then you should make sure we have your most up-to-date e-mail address! The SSF is starting to share more information via e-mail, from news about the SSF and Sjögren’s, to information about the latest treatments and medicines, to local Support Group updates and more. So contact us at ssf@sjogrens.org to be certain we have your latest e-mail address in our database, and then keep an eye out in your Inbox for Sjögren’s news.

Just like all information you give the Foundation, your e-mail address will remain private and will never be given or sold to an outside organization.
**Oral Health News**

**Another Reason to Take Vitamin D?**

We have all heard the news about the link between low Vitamin D levels and the development of autoimmune diseases, including Sjögren's (see two *Sjögren's Quarterly* articles – in the Fall 2012 issue by Yehuda Shoenfeld, MD and Nancy Agmon-Levin, MD and in the Summer 2007 issue by Jeffrey W. Wilson, MD). Now there might be another reason to ensure that your Sjögren’s patients are getting a sufficient amount of Vitamin D. A review published in December in *Nutrition Reviews* found that Vitamin D might help lower the rate of dental caries. Philippe Hujoel, PhD, DDS, MSD, MS, of the University of Washington School of Dentistry and School of Public Health in Seattle, Washington, executed a systematic review of 24 controlled clinical trials from the 1920s to the 1980s and concluded that Vitamin D was associated with an approximately 50 percent reduction in the incidence of tooth decay in children. The data analysis identified Vitamin D as a promising caries-preventive agent that leads to better mineralization of teeth and bones. While studies have not been carried out directly in Sjögren’s patients, this finding might provide an additional reason to check Vitamin D levels in Sjögren’s patients.


**Friends of the NIDCR Conference – SSF CEO Moderates Patient Advocacy Panel**

A new feature debuted during the Friends of the National Institute of Dental and Craniofacial Research (FNIDCR) annual conference in December with a Patient Advocacy Panel Discussion entitled “From Bench to Bedside: A Focus on the Bedside!” Moderated by Steven Taylor, SSF CEO, the panel included members of the patient advocacy community that is served by the NIDCR at the National Institutes of Health. The NIDCR has long recognized and highlighted the importance of the ultimate beneficiary of the medical and scientific research it supports – the patient. To showcase this vital focus, FNIDCR invited members of the patient advocacy community to talk about the diseases and conditions represented by their organizations and the importance of NIDCR in providing hope for the future through its research programs.

SSF Vice President of Research Kathy Hammitt chaired the conference, “Exploring the Research Interface between Academia, Industry, Practice & Patient.” The day included a luncheon keynote address by NIDCR Director Martha Somerman on “Leading Edge Frontiers in Oral and Craniofacial Research;” dinner keynote speaker, Mary Woolley, President of Research!America, whose topic was “Fiscal Cliff-diving is a Deadly Proposition for Research;” NIDCR grantees; and an industry round table. U.S. Congressman Paul Gosar, DDS and R-AZ received the Friends of NIDCR Outstanding Lifetime...
Achievement Award and, while noting the nation’s difficult financial condition also recognized the importance of a national commitment to research.

**Sequestration Would Devastate Research**

All of NIH faces major economic uncertainty as sequestration (across-the-board cuts for the federal government) is set to take place on March 1 if Congress does not reduce the deficit. In addition, the current continuing resolution that is keeping the federal government going will end March 27 unless continued or a FY2013 budget is passed. If sequestration takes place, the NIH would be cut by 8.2% or $2.518 billion dollars with as many as 2,300 fewer grants funded. This could have devastating ripple effects for years to come on medical and scientific research carried out in the U.S.

**NIEHS Job Announcement**

The National Institute of Environmental Health Sciences (NIEHS) at the National Institutes of Health (NIH) has announced that it is looking for a Director of Clinical Research to lead clinical-translational research at the senior investigator (tenure-eligible) level. The position can include an independent laboratory. NIEHS supports research on potential environmental triggers into autoimmune disease and includes the Environmental Autoimmunity Group. The SSF is a member of the Friends of NIEHS. Applications are due February 28, 2013. More information is available at http://niehs.nih.gov/careers/jobs/director_clinical_research_program_dir_1301.cfm.

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If you would like to receive information on how you can Leave a Legacy to support the Sjögren’s Syndrome Foundation’s critical research initiatives or to support one of our many other programs, please contact Steven Taylor at 800-475-6473.

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precise “trigger” for initiating autoimmune disorders, development of early detection devices and prevention measures, and formulating new generations of effective symptom-managing products for SS patients that protect the secretory glands from further damage.

**References**

Join Team Sjögren’s in Nashville, the home of country music...  
...and the Country Music Marathon and Half-Marathon

Join Team Sjögren’s and train to run or walk in the 2013 Country Music Marathon and Half-Marathon in Nashville on April 27, 2013.

We are looking for 30 inspired individuals to join us as we begin to train for this challenge. We understand that not all Sjögren’s patients are able to run or walk in a marathon, so we hope you will help us recruit someone else — your husband, wife, sister, cousin, daughter, son or friend — and have them run in your honor!

By signing up to join Team Sjögren’s, you not only will receive world-class training but also leadership and mentorship from past runners and staff. You will receive coaching from our Team Trainer as well as our Team Nutritionist. The staff of the SSF will help guide you through the entire process and ensure you are ready to complete either the 13.1- or 26.2-mile course!

In addition to raising awareness for Sjögren’s, you also will be helping to raise crucial funds for Sjögren’s research and education.

Just imagine the difference you will be making as you run or walk in honor of all Sjögren’s patients!

To learn more about Team Sjögren’s, contact Steven Taylor at 800-475-6473, ext. 211, or staylor@sjogrens.org
Lubricate the ocular surface.

Protect the exposed surface of the eye from infections. Clear vision depends on even

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patients and their families, increases public and
cation, and awareness. SSF supports and educates

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Providing the Foundation with one more voice to increase

Members-only discounts on a variety of products and

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Join the SSF today and receive these great mem-

support its ongoing programs, including support groups,
of which help in the fight to conquer Sjögren's syndrome.

registration for our educational conferences.

articles, our online product guide, and daily survival tips.

syndrome and the Foundation's activities.

individuals and fellow Sjögren's syndrome patients are

local support groups. These knowledgeable and empathetic

information on Sjögren's syndrome, practical tips for daily

syndrome, this monthly newsletter contains the latest

living, and answers to medical questions from the experts.

Figure 1

Normal healthy tears

Diagnosing Dry Mouth

a change in salivary function and the severity of any sali-

It is important to determine if dry mouth is caused by

A complete medical and prescription drug history is taken.

other sites (eyes, nose, throat, skin, vagina) is documented.

Figure 2

disease is present. The average time

do not recognize that a systemic
treat each symptom individually and

can involve several body systems,

medical conditions such as lupus,

or misdiagnosed. The symptoms of

Sjögren's syndrome often is undiagnosed

Symptoms vary from person to person but may

with Sjögren's syndrome

may be helpful for people

Healthcare professionals: Call to order complimentary

materials to share with your patients!

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Always go to the emergency room if:

- You are having chest pain, even if you think it may be severe GERD or esophageal spasm. It is best to let the experts determine the cause.
- You have any signs of a stroke – numbness/tingling or inability to move an extremity, inability to speak, loss of consciousness, visual disturbance or loss of vision.

Additional important information:

- Do not attempt to drive yourself to the emergency room if the above occur. It is best to call 911 so your condition can be evaluated by a healthcare professional as soon as possible. If you are alone and able, call a family member or friend to be with you and accompany you to the ER.
- Remember to bring your insurance cards, photo id and a means to pay your co-pay.
- Take your oral and ocular products and the remainder of your daily medications with you. Do not take any medications while in the ER or while waiting to be seen without permission from your doctor.
- Take a copy of your medical history, medication list and list of your key doctors and their contact information with you.
- Tell the nurses and doctor that you have Sjögren’s. If they don’t know what Sjögren’s is, tell them it is a lupus-like disease.
- If you have problems other than the above, you may still need to go to the emergency room. Call your doctor’s office or the doctor on call after hours and on weekends and report your symptoms. They will help you determine whether an emergency room visit is necessary.
- Remember that the most critical patients will be seen first in the emergency room (i.e. chest pain, stroke, trauma), so you may have to wait a considerable amount of time to be taken to a room and be seen by a doctor.
- Be aware of other care providers in your area to treat non-emergency care needs. An urgent care center or orthopedic after-hours clinic may be a more timely and cost-effective manner to get your health concerns addressed. Bring the same information you would bring to the emergency room to these facilities.
New Product

Introducing a New Product for Dry Mouth!

A new lozenge for dry mouth has been launched by MedActive Oral Pharmaceuticals, LLC. The Natural Spring Oral Relief Lozenges are free of the following:

- Artificial dyes and coloring
- Sugar
- Alcohol
- Gluten
- Sodium

MedActive states that the lozenge enhances saliva and conditions the soft mucosal tissues of the mouth and provides quick relief for the dry mouth and often extreme sensitivity to flavors that Sjögren’s patients can experience. The lozenges are available online at www.medactive.com and also can be purchased in the northeastern U.S. through Independent Retail Pharmacies. Visit the website for more information.